DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

m49934

Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

CBER-01-006

NOV 30 2000

WARNING LETTER

Certified Mail
Return Receipt Requested

Alan L. Buchman, M.D.
Clinical Investigator
676 N. St. Clair, Suite 880
Chicago, IL 60611

Dear Dr. Buchman:

During an inspection ending on June 23, 2000, Ms. Andrea A. Branche and Ms. Tricia Y. Samaniego, investigators with the Food and Drug Administration (FDA), met with Dr. Joseph H. Sellin and members of the staff at the University of Texas-Houston Health Science Center, to review your conduct of a clinical study entitled [redacted] is the sponsor of the clinical trial. The inspection is part of FDA's Bioresearch Monitoring Program that includes inspections designed to audit the conduct of research involving investigational drugs.

The deficiencies noted during the inspection are listed on the Form FDA 483, Inspectional Observations, that was presented and discussed with Dr. Joseph Sellin and other representatives of the University of Texas-Houston Health Science Center at the conclusion of the inspection (enclosed). Based on our review of the information from the inspection, we identified deviations from applicable federal regulations as published in Title 21, Code of Federal Regulations, Parts 312 and 50 [21 CFR 312 and 50]. The applicable provisions of the CFR are cited for each violation.

1. **Failure to fulfill the general responsibilities of investigators [21 CFR 312.60 and Part 50].**

   On 5/28/98 and 6/11/98, you signed Forms FDA 1572 Statement of Investigator, in which you agreed to fulfill the requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

   Our investigation revealed that you did not fulfill your obligations as a clinical investigator in the use of investigational new drugs for the following reasons:

a. You did not personally conduct or supervise this study, a commitment you agreed to by signing the Form FDA 1572, as evidenced by the following:

   i. Two unlicensed staff members conducted physical examinations for the study. Dr. Mohammed Awal and Dr. Mir Sohel participated as study coordinators and are not licensed physicians in the United States. They conducted protocol required screening physical examinations for subjects #906, 912, 913, 914, and protocol required on-study physicals for subjects #901, 907, 912, and 913. The study coordinators conducted the physicals from 9/98 until 2/2000.

   ii. One study coordinator entered on-study physical exam results for portions of the exam he did not conduct.

   Physical exams conducted by Dr. Mohammed Awal did not include a physical examination (such as, palpations, opthalmoscopic, otoscopic, digital exam of the eyes, ears, breast, genitourinary/pelvic, rectal, musculoskeletal, or neurologic system) as required by the protocol. Instead, Dr. Awal, the study coordinator, entered a result of normal on the case report forms for all subjects examined during this period based on a visual examination of these areas.

b. You misrepresented your presence at the institution by signing and dating source documents and consent forms on days you were, in fact, absent from the institution. For example,

   i. You signed and dated source data for physicals conducted on 12/11/98 (subject #906), 5/13/99 (subjects #909 and #910), and 9/10/99 (subject #912). The institution attendance records for this period indicate you were not present on these dates.

   ii. You signed and dated subjects' informed consents on dates when you were absent from the clinical site. As a result, informed consent was not properly obtained for the following subjects:

   subject #906 (12/11/98)
   subject #909 (5/13/99)
   subject #910 (5/13/99)
   subject #912 (9/10/99)

c. You failed to provide the names of all sub-investigators to the sponsor on the Form FDA 1572. You failed to provide to the sponsor the names of either Mir Sohel or Mohammed Awal as sub-investigators on the Form FDA 1572, until the updated version signed by you on 1/6/00 when Mohammed Awal is included. By these omissions, you failed to give the sponsor the opportunity to assess the qualifications of these sub-investigators.

2. **Failure to prepare and maintain complete and accurate case histories [21 CFR 321.62(b)].**

   There is no source documentation available for screening and on-study physicals conducted by the study coordinators.

As evidenced by the deviations noted above, the records at your site indicate a serious failure to fulfill your responsibilities as principal investigator including supervision of study personnel. Staff who were delegated the authority to perform certain functions were not adequately credentialed, trained, or monitored. Although authority may be delegated, the principal investigator is ultimately responsible for study conduct.

Based on the deviations noted above, we recommend that you complete a course in good clinical practices (GCPs). Given that the above deviations occurred at the University of Texas-Houston Health Science Center, it is essential that you, as clinical investigator responsible for the conduct of clinical trials, assure that all sub-investigators and all other study personnel who participate in the conduct of clinical trials under your supervision at Northwestern University Medical School are adequately trained in good clinical practices and are properly supervised.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study. It is your responsibility to ensure adherence to each requirement of the law and applicable regulations.

Please notify this office in writing, within 15 business days of receipt of this letter, of the specific actions you have taken to correct the noted violations, including an explanation of each step you plan to take to prevent a recurrence of similar violations. If corrective action cannot be completed within 15 business days, state the reason for the delay and the time within which corrections will be completed.

Failure to achieve prompt correction may result in enforcement action without further notice. These actions could include initiation of clinical investigator disqualification proceedings that may render a clinical investigator ineligible to receive investigational drugs, a clinical hold, or termination of an investigational new drug application (IND).

Please send your written response to:

Debra Bower (HFM-664)
FDA/Center for Biologics Evaluation and Research
Division of Inspections and Surveillance
1401 Rockville Pike
Rockville, MD 20852-1448

Please send a copy of your response to FDA's Dallas District Office, Director, Compliance Branch, 3310 Live Oak Street, Dallas, TX 75204. If you require additional time to respond, or have any questions concerning this matter, please contact Ms. Bower at (Tel.) 301-827-6221.

Sincerely,

Steven A. Masiello
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation
and Research

Enclosure
Form FDA 483 dated 6/23/2000

cc:

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cc (continued):